

CURRENT STATUS OF CLAIMS WITH CLAIM AMENDMENTS

Please cancel claims 1-3.

1-3. (Canceled).

4. (Presently amended) A botulinum toxin serotype A (BoNT/A) substrate, comprising:

(a) a donor fluorophore;  
(b) an acceptor having an absorbance spectrum overlapping the emission spectrum of said donor fluorophore; and  
(c) a BoNT/A recognition sequence comprising a cleavage site, wherein said cleavage site intervenes between said donor fluorophore and said acceptor and wherein, under the appropriate conditions, resonance energy transfer is exhibited between said donor fluorophore and said acceptor, said substrate having a length of amino acids selected from the group consisting of 19 amino acids, 20 amino acids, 21 amino acids, 22 amino acids, 69 amino acids and 72 amino acids.

5. (Original) The substrate of claim 4, comprising at least six consecutive residues of SNAP-25, said six consecutive residues comprising Gln-Arg, or a peptidomimetic thereof.

6. (Previously presented) The substrate of claim 5, comprising at least six consecutive residues of a human SNAP-25, said six consecutive residues comprising Gln197-Arg198, or a peptidomimetic thereof.

7. (Original) The substrate of claim 6, comprising the amino acid sequence Glu-Ala-Asn-Gln-Arg-Ala-Thr-Lys (SEQ ID NO: 1), or a peptidomimetic thereof.

8. (Original) The substrate of claim 6, comprising residues 187 to 203 of human SNAP-25 (SEQ ID NO: 2), or a peptidomimetic thereof.

9-44. (Canceled)

45. (Presently amended) The substrate of claim 4 any of claims 1, 2, 3 or 4, wherein said substrate can be cleaved with an activity of at least 1 nanomole/minute/milligram toxin.

46. (Presently amended) The substrate of claim 4 any of claims 1, 2, 3 or 4, wherein said substrate can be cleaved with an activity of at least 20 nanomole/minute/milligram toxin.

47. (Presently amended) The substrate of claim 4 any of claims 1, 2, 3 or 4, wherein said substrate can be cleaved with an activity of at least 50 nanomole/minute/milligram toxin.

48. (Presently amended) The substrate of claim 4 any of claims 1, 2, 3 or 4, wherein said substrate can be cleaved with an activity of at least 100 nanomole/minute/milligram toxin.

49. (Presently amended) The substrate of claim 4 any of claims 1, 2, 3 or 4, wherein said substrate can be cleaved with an activity of at least 150 nanomole/minute/milligram toxin.

50. (Presently amended) The substrate of claim 4 [[1]], wherein said acceptor is an acceptor fluorophore.

51. (Original) The substrate of claim 50, wherein said acceptor fluorophore has a fluorescent lifetime of at least 1 microsecond.

52. (Presently amended) The substrate of claim 4 [[1]], wherein said acceptor is non-fluorescent.

53. (Presently amended) The substrate of claim 4 [[1]], wherein said donor fluorophore is fluorescein.

54. (Canceled)

55. (Presently amended) The substrate of claim 4 [[1]], wherein said donor fluorophore is 4-(4-dimethylaminophenylazo)benzoic acid (DABCYL) **DABCYL**.

56. (Canceled)

57. (Presently amended) The substrate of claim 4 or claim 53 1, claim 53, or claim 54, wherein said acceptor is tetramethylrhodamine.

58. (Presently amended) The substrate of claim 4 [[1,]] or claim 55, wherein said acceptor is 5-[(2-aminoethyl)amino]-naphthalene-1-sulfonic acid (EDANS) **EDANS**.

59. (Presently amended) The substrate of claim 4 or claim 53 1, claim 53 or claim 54, wherein said acceptor is a non-fluorescent acceptor.

60. (Presently amended) The substrate of claim 4 [[1]], which is a peptide or peptidomimetic having at most 100 residues.

61. (Original) The substrate of claim 60, which is a peptide or peptidomimetic having at most 50 residues.

62. (Original) The substrate of claim 61, which is a peptide or peptidomimetic having at most 40 residues.

63. (Original) The substrate of claim 62, which is a peptide or peptidomimetic having at most 20 residues.

64. (Previously presented) The substrate of claim 50, wherein said donor fluorophore and said acceptor fluorophore are separated by at most fifteen residues.

65. (Original) The substrate of claim 64, wherein said donor fluorophore and said acceptor fluorophore are separated by at most ten residues.

66. (Original) The substrate of claim 65, wherein said donor fluorophore and said acceptor fluorophore are separated by at most eight residues.

67. (Original) The substrate of claim 66, wherein said donor fluorophore and said acceptor fluorophore are separated by at most six residues.

68-95. (Canceled)

Please add the following new claims:

96. (New) The substrate of claim 4, wherein said substrate has a length of 19 amino acids.

97. (New) The substrate of claim 4, wherein said substrate has a length of 20 amino acids.

98. (New) The substrate of claim 4, wherein said substrate has a length of 21 amino acids.

99. (New) The substrate of claim 4, wherein said substrate has a length of 22 amino acids.

100. (New) The substrate of claim 4, wherein said substrate has a length of 69 amino acids.

101. (New) The substrate of claim 4, wherein said substrate has a length of 72 amino acids.

102. (New) A botulinum toxin serotype A (BoNT/A) substrate, comprising:

(a) a donor fluorophore;  
(b) an acceptor having an absorbance spectrum overlapping the emission spectrum of said donor fluorophore; and  
(c) a BoNT/A recognition sequence comprising a cleavage site, said BoNT/A recognition sequence comprising at least six consecutive residues of human SNAP-25 (SEQ ID NO: 2), said six consecutive residues comprising Gln197-Arg198 or a peptidomimetic thereof, wherein said cleavage site intervenes between said donor fluorophore and said acceptor and wherein, under the appropriate conditions, resonance energy transfer is exhibited between said donor fluorophore and said acceptor.

103. (New) The substrate of claim 102, comprising the amino acid sequence Glu-Ala-Asn-Gln-Arg-Ala-Thr-Lys (SEQ ID NO: 1), or a peptidomimetic thereof.

104. (New) The substrate of claim 102, comprising the amino acid sequence Ser-Asn-Lys-Thr-Arg-Ile-Asp-Glu-Ala-Asn-Gln-Arg-Ala-Thr-Lys-Met-Leu (SEQ ID NO: 30), or a peptidomimetic thereof.

105. (New) The substrate of any of claims 102, 103 or 104, wherein said substrate can be cleaved with an activity of at least 1 nanomole/minute/milligram toxin.

106. (New) The substrate of any of claims 102, 103 or 104, wherein said substrate can be cleaved with an activity of at least 20 nanomole/minute/milligram toxin.
107. (New) The substrate of any of claims 102, 103 or 104, wherein said substrate can be cleaved with an activity of at least 50 nanomole/minute/milligram toxin.
108. (New) The substrate of any of claims 102, 103 or 104, wherein said substrate can be cleaved with an activity of at least 100 nanomole/minute/milligram toxin.
109. (New) The substrate of any of claims 102, 103 or 104, wherein said substrate can be cleaved with an activity of at least 150 nanomole/minute/milligram toxin.
110. (New) The substrate of claim 102, wherein said acceptor is an acceptor fluorophore.
111. (New) The substrate of claim 110, wherein said acceptor fluorophore has a fluorescent lifetime of at least 1 microsecond.
112. (New) The substrate of claim 102, wherein said acceptor is a non-fluorescent acceptor.
113. (New) The substrate of claim 102, wherein said donor fluorophore is fluorescein.
114. (New) The substrate of claim 102, wherein said donor fluorophore is DABCYL.
115. (New) The substrate of claim 102 or 113, wherein said acceptor is tetramethylrhodamine.
116. (New) The substrate of claim 102 or 114, wherein said acceptor is EDANS.
117. (New) The substrate of claim 113, wherein said acceptor is a non-fluorescent acceptor.
118. (New) The substrate of claim 102, which is a peptide or peptidomimetic having at most 100 residues.

119. (New) The substrate of claim 118, which is a peptide or peptidomimetic having at most 50 residues.

120. (New) The substrate of claim 119, which is a peptide or peptidomimetic having at most 40 residues.

121. (New) The substrate of claim 120, which is a peptide or peptidomimetic having at most 20 residues.

122. (New) The substrate of claim 102, wherein said donor fluorophore and said acceptor fluorophore are separated by at most fifteen residues.

123. (New) The substrate of claim 122, wherein said donor fluorophore and said acceptor fluorophore are separated by at most ten residues.

124. (New) The substrate of claim 123, wherein said donor fluorophore and said acceptor fluorophore are separated by at most eight residues.

125. (New) The substrate of claim 124, wherein said donor fluorophore and said acceptor fluorophore are separated by at most six residues.

126. (New) A botulinum toxin serotype A (BoNT/A) substrate, comprising:

- (a) a donor fluorophore;
- (b) an acceptor having an absorbance spectrum overlapping the emission spectrum of said donor fluorophore; and
- (c) a BoNT/A recognition sequence comprising a cleavage site, wherein said cleavage site intervenes between said donor fluorophore and said acceptor and wherein, under the appropriate conditions, resonance energy transfer is exhibited between said donor fluorophore and said acceptor, wherein said donor fluorophore or said acceptor is genetically encoded.

127. (New) The substrate of claim 126, wherein said donor fluorophore is genetically encoded.

128. (New) The substrate of claim 126, wherein said acceptor is genetically encoded.

129. (New) The substrate of claim 126, wherein said donor fluorophore and said acceptor are genetically encoded.

130. (New) The substrate of claim 126, comprising at least six consecutive residues of SNAP-25, said six consecutive residues comprising Gln-Arg.

131. (New) The substrate of claim 130, comprising at least six consecutive residues of a human SNAP-25, said six consecutive residues comprising Gln197-Arg198.

132. (New) The substrate of claim 131, comprising the amino acid sequence Glu-Ala-Asn-Gln-Arg-Ala-Thr-Lys (SEQ ID NO: 1).

133. (New) The substrate of claim 131, comprising residues 187 to 203 of human SNAP-25 (SEQ ID NO: 2).

134. (New) The substrate of claim 126, wherein said substrate can be cleaved with an activity of at least 1 nanomole/minute/milligram toxin.

135. (New) The substrate of claim 126, wherein said substrate can be cleaved with an activity of at least 20 nanomole/minute/milligram toxin.

136. (New) The substrate of claim 126, wherein said substrate can be cleaved with an activity of at least 50 nanomole/minute/milligram toxin.

137. (New) The substrate of claim 126, wherein said substrate can be cleaved with an activity of at least 100 nanomole/minute/milligram toxin.

138. (New) The substrate of claim 126, wherein said substrate can be cleaved with an activity of at least 150 nanomole/minute/milligram toxin.

139. (New) The substrate of claim 126, wherein said acceptor is an acceptor fluorophore.

140. (New) The substrate of claim 139, wherein said acceptor fluorophore has a fluorescent lifetime of at least 1 microsecond.

141. (New) The substrate of claim 126, which is a peptide having at most 100 residues.
142. (New) The substrate of claim 141, which is a peptide having at most 50 residues.
143. (New) The substrate of claim 142, which is a peptide having at most 40 residues.
144. (New) The substrate of claim 143, which is a peptide having at most 20 residues.
145. (New) The substrate of claim 144, wherein said donor fluorophore and said acceptor fluorophore are separated by at most fifteen residues.
146. (New) The substrate of claim 145, wherein said donor fluorophore and said acceptor fluorophore are separated by at most ten residues.
147. (New) The substrate of claim 146, wherein said donor fluorophore and said acceptor fluorophore are separated by at most eight residues.
148. (New) The substrate of claim 147, wherein said donor fluorophore and said acceptor fluorophore are separated by at most six residues.